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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,748	02/27/2001	Adi Kimchi	KIMCHI 2A	4171

1444 7590 06/02/2003

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EXAMINER	
MONSHIPOURI, MARYAM	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/719,748	Kimchi et al.
Examiner	**Art Unit**
Maryam Monshipouri	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20, 23, 24, and 27-36* is/are pending in the application.

4a) Of the above, claim(s) *29 and 30* is/are withdrawn from consideration.

5)☒ Claim(s) *13, 28, and 35* is/are allowed.

6)☒ Claim(s) *1, 2, 6, 8, 9, 11, 12, 14-20, 23, 24, 27, 31, and 32* is/are rejected.

7)☒ Claim(s) *3-5, 7, 10, 33, 34, and 36* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 21-22, 25-26 have been canceled. Claims 1, 8, 13, 27-28 and newly presented claims 31-36 are still at issue and are present for examination. Claims 29-30 are withdrawn as drawn to non-elected invention.

In view of applicant's filing of In *re Katz-type* declaration (paper #16) Group II invention directed to claims 2-7, 9-12, 14-19, 23-24 are hereby rejoined with the elected invention.

DETAILED ACTION

1. Claims 1-20, 23-24 and 27-36 are under examination. Applicants' arguments filed on 11/20/2002 (paper # 13), 1/21/2003 (paper #14) and 3/25/2003 (Paper # 15), have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

2. ***Claim Objections***

3. Claim 19 is objected to because of the following informalities: the term "ay of claims 2" does not make sense. applicant is advised to rewrite said term as " claim 2". Appropriate correction is required.

4. Claim 20 is objected to because of the following informalities: the phrase " any one of claim 1" is incorrect. Applicant is advised to rewrite said phrase as "claim 1" . Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 11-12, 14-15, 16-17, 18-20, 24 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2 and fragments thereof which are capable of inducing cell death, does not reasonably provide enablement for at least 85 % homologs of said fragments which are capable of inducing cell death shown claim 1 (D), or 85% or higher homologs of fragments of claim 1 (E) wherein said fragment can inhibit the ability of polypeptides of claim 1(A) or (B) to induce cell death, shown in claim 1(F).

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The disclosure fails to teach which residues in polypeptide homologs of claims 1(D) and 1(F) should be retained in order to preserve the properties such as " inducing cell death" or "lacking the capability of inducing cell death while being able to inhibit polypeptides of claim 1(A)-(B) to induce cell death", respectively. No examples of such homologs are provided either. Current state of the art indicates that fragment homologs of claim 1(D) and (1F) is not necessarily

going to induce cell death or lack the capability of inducing cell death while being able to inhibit polypeptides of claim 1(A)-(B) to induce cell death, respectively.

Therefore to lack of sufficient examples and guidance provided in the disclosure and in view of unpredictability of prior art as to which fragments of claimed homologs are likely to retain the properties of polypeptides of claims 1(D) and 1(F), one of skill in the art has to go through the burden of undue experimentation in order to screen for the polypeptides of claims 1(D) and 1(F) and as such the claims go beyond the scope of the disclosure.

Since the polypeptides of claim 1, 31-32 are not enabled, their encoding sequences (claim 2), vectors, host cells and compositions comprising said DNA sequences (claims 18-20) are not enabled either.

In claims 14-15, applicant is reciting DNA molecules that need to **comprise** a DNA region encoding merely residues 320-360 of SEQ ID NO:2 or at least 85% homologs of said amino acid fragment with capability of inducing cell death. In order words such claims read on for example DNA molecules of 10,000 nucleotides which need to comprise merely 120 nucleotides of SEQ ID NO:1 in order to be within the scope of this invention.

Again considering the re Wands Factors shown above, applicant does not teach what other structural requirements must be retained in claims DNA molecules such that they can encode products which fold in the appropriate conformation such that they can induce cell death. No examples of such DNA molecules are provided either. Current state of prior art indicates that

any large DNA molecule which embraces a small DNA fragment of a DNA molecule capable of encoding a fragment with activity is not necessarily going to encode a product with said activity.

Therefore, due to lack of sufficient structural information and examples provided in the disclosure and due to unpredictability of prior art as to the structural requirements of claimed DNA molecules such that they can encode products with capability of inducing cell death one of skill in the art has to go through the burden of undue experimentation in order to screen for DNA molecules that are within the scope of this invention.

With respect to claims 11-12 and 16-17, it should be noted that claimed DNA sequence do not recite any function. Applicant is advised to review the *re Wand* parameters recited above.

The disclosure does not provide any information about the critical residues in DNA sequences that can hybridize to nucleotides 98-886 or nucleotides 1022-1141 of SEQ ID NO:1 under any stringent conditions, which must be retained in order to encode a product with function. No examples of such DNA homologs are provided either. Current state of prior art indicates that any DNA sequence that can hybridize to that encoding a useful fragment with a specific activity is not necessarily capable of encoding a product with a function identical to said fragment.

Therefore due to lack of sufficient guidance and examples in the prior art and due to unpredictability of prior art has to which DNA homologs are capable of encoding products with activities identical to residues 13-275 and 321-360 of SEQ ID NO:2, one of skill in the art has to

go through the burden of undue experimentation in order to screen for DNA homologs that are within the scope of this invention and as such the claims go beyond the scope of the disclosure.

With respect to claim 24, applicant is reminded that even though the claim is enabled for an "in vitro" method of neutralizing messenger RNA (mRNA) molecule comprising the step of contacting the single stranded RNA molecule of claim 23, with the mRNA in order to neutralize it by hybridization, it does not provide enablement for " in vivo" methods of neutralizing said mRNA molecule.

As applicant is aware claim 24 is very broad and reads on "in vivo" methods of treatment of diseases or disorders caused by DAP kinase expression in live organisms. Such methods rely on "in vivo" delivery of antisense to specific tissue in said organism in order to inhibit translation of mRNA. However, applicant has not provided which gene delivery vehicles, at what concentration and under which circumstances are likely to be successful in neutralizing DAP kinase mRNA " in vivo" in the disclosure. No examples of said delivery methods and conditions are provided either. Current state of the art does not provide sufficient knowledge to allow selection of methods which utilize antisense molecules that can successfully neutralize said mRNA's in organisms, based merely on structural information of DAP kinase gene.

Therefore, considering *re Wands* factors above, due to lack of sufficient informtion and examples provided in the disclosure and due to unpredicatbility of prior art as to which methods are likely to neutrilize DAP kinase mRNA "in vivo" with potential success, one of skill in the art has to go through the burden of undue experimentation in order to screen for those methods of

use of antisense molecules that are within the scope of this invention (claim 24) and as such the claim goes beyond the scope of the disclosure.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 8-9, 11, 12, 27 are rejected under 35 U.S.C. 102(b) or 102 (a) as being anticipated by Deiss (cited previously) or Akira (cited previously). As mentioned in the previous office action, both Deiss and Akira teach a DNA sequence comprising a region encoding a DAP kinase that can reasonably be assumed to have at least 85% identity to residues 13-275 of SEQ ID NO:2 (and their expression products), or sequences that can hybridize to said DNA sequence under moderately or highly stringent conditions, anticipating claims 1, 8-9, 11-12. In traversal of this rejection applicant argues the following : (1) that even if the 83.7% query match" of Deiss

with residues 13-275 of SEQ ID NO:2 and the 82.4% "query match" of Akira are interpreted as "sequence identity", they simply do not anticipate the required feature of "at least 85% sequence identity" as recited in the rejected claims.

(2) The "query match" indicated in the sequence alignments cited by the examiner is not equivalent to sequence identity". As shown in the sequence alignments, a 263 residue query sequence is aligned with a 263 residue sequence of residues 13-275 of SEQ ID NO:2. There are no gaps in the aligned sequences of exactly the same length. Consequently, the percentage sequence identity is unambiguously the number of exact matches (209) residues divided by the total number of residue positions aligned (263 residues) and then multiplied by 100 to give both for Akira and Deiss 79.5% sequence identity. Hence, according to applicant, Deiss or Akira cannot anticipate the presently claimed invention.

These arguments were fully considered but were found **unpersuasive**. With respect to applicant's **first** argument, the examiner maintains that sequence identities displayed by Deiss and Akira remain to anticipate the invention because applicant did not recite exactly which software and which analysis parameters were used in order to obtain 85% sequence identity to SEQ ID NO:2 in the claims. Applicant is well aware that percent identity in the absence of recitation of exact software and analyses parameters used, cannot be exact and precise. Again, the examiner maintains that the art cited displays sequence identities that are basically at least 85% to SEQ ID NO:2 of this invention unless applicant provides evidence that using his/her particular

software and analysis parameters of the cited art gives sequence identities lower than 85% to SEQ ID NO:2 of this invention.

With regard to applicant **second** argument, it should be pointed out that applicant is imposing his new interpretation of sequence identity, which seems to be tailor made to overcome this rejection, on the examiner. In pages 9-10 of the disclosure applicant discusses how percentage identities were determined. Applicant refers to Clustal-X program and GDAP programs and mentions the types of analysis parameters used. These discussions are not supporting applicant's allegedly unambiguous interpretation of sequence identity provided instantly.

In order to overcome this rejection applicant is advised to possibly attempt the following : **(I)** align the sequences of Deiss and Akira with SEQ ID NO:2 using the sequence identity information provided in the disclosure and demonstrate that indeed they are less than 85% and **(II)** recite the software and analyses parameters used into relevant claims. Under such circumstances the rejection may be withdrawn.

8. Claim 11 and 6 is rejected under 35 U.S.C. 102(e) as being anticipated by Akira et al. (U.S. Patent No. 5,958,748, 9/1999). It is noted that applicant claims priority to a provisional application. However said provisional does not disclose any DNA sequences that can hybridize to residues 98-886 o SEQ ID NO:1. Hence, the earliest priority date that applicant can benefit from, with regards to this claim is 6/15/1999. Based on this priority date, Akira discloses a DNA sequence (see its SEQ ID NO:4) the comprises a region having 76.1%, and 76.7% local

similarity (see the attached alignment), to nucleotides 62-1141 and 98-886 of SEQ ID NO:1 of this invention, respectively. Said sequences can hybridize to claimed fragments of SEQ ID NO:1, under moderately stringent conditions.

9. Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al. (Database EST, Accession No. W82116, 9/1996). Marra tecahes an mRNA sequence that has 90.4% homology to a region of SEQ ID NO:1 (see the attached alignment). Absent to contrary, it is beleived that Marra's single stranded sequence is capable of hyrbidizing to mRNA of SEQ ID NO:1 of this invention and can prevent its translation into SEQ ID NO:2, anticipating claim 23.

Allowable Subject Matter

10. Claims 3-5, 7, 10, and 33-34, 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. This is because SEQ ID NO:2, fragment of SEQ ID NO:2 consisting of residues 13-275 with their specifically claimed functions as well as DNA sequences consisting of residues 62-1141 or 98-886 of SEQ ID NO:1, its specifically claimed homologs with specifically claimed function are free of prior art. Further the prior art does not teach or suggest preparing such specifically claimed products. Hence, said products are also non-obvious.

Claims 13, 28 and 35 are allowed. This is because a polypeptide consisting of residues 321-360 of SEQ ID NO:2 and specifically claimed homologs thereof with inhibit the ability of

SEQ ID NO:2 to induce cell death are free of prior art. Further the prior art does not teach or suggest preparing such specifically claimed polypeptide sequences. Hence said polypeptides are novel and non-obvious. Since said polypeptides are novel and non-obvious compositions comprising said polypeptides are also novel and non-obvious.

11. Inquiries concerning this communication or earlier communications from the Examiner should be directed to Maryam Monshipouri, Ph.D. whose telephone number is (703) 308-1083.

The Examiner can normally be reached daily from 8:30 A.M. to 5:00 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. P. Achutamurthy, can be reached at (703) 308-3804. The OFFICIAL fax number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

M. Monshipouri

MARYAM MONSHIPOURI, PH.D.
PRIMARY EXAMINER